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10/510,557	10/07/2004	Virginia K Walker	AF-0022	4185

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EXAMINER
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RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
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1652

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/04/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/510,557	<b>Applicant(s)</b> WALKER ET AL.	
	<b>Examiner</b> Delia M. Ramirez	<b>Art Unit</b> 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 and 14-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/7/04;3/8/07</u>  | 6) <input type="checkbox"/> Other: _____                          |

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## DETAILED ACTION

### *Status of the Application*

Claims 1-20 are pending.

It is noted that the examination of the instant application has been assigned to a different Examiner in Group Art Unit 1652.

Applicant's election with traverse of Group I, claims 1-13, 14-20 drawn to a method for inhibiting clathrate hydrate plug formation, as submitted in a communication filed on 11/13/2006 is acknowledged.

Applicant's traverse is on the grounds that all claims were searched during the PCT phase of the instant application. Thus, a conclusion of lack of unity contradicts the search conducted by the PCT Examiner. In addition, Applicant argues that since claim 13 was searched, inclusion of Group II would not place an additional burden on the Office.

Applicant's arguments have been fully considered but are not deemed persuasive to withdraw the restriction requirement. The Examiner acknowledges the search conducted by the International Search Authority. However, even if the International Search Authority found unity of invention regarding the instant claims, it is noted that according to 37 CFR 1.499, if the Examiner finds that a national stage application lacks unity of invention under 37 CFR § 1.475, the examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted. Such requirement may be made before any action on the merits but may be made at any time before the final action at the discretion of the Examiner. In the instant case, as indicated in the restriction requirement, the inventions of Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2 they lack the same or corresponding special technical feature. The special technical feature of Invention I is a method for inhibiting clathrate formation whereas the special technical feature of Invention II is a method for screening clathrate hydrate inhibitors. These

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methods have different steps and produce different results. In addition, Inventions I-II do not have unity of invention according to 37 CFR 1.475 as they do not correspond to any of the combinations set forth therein as having unity of invention. Furthermore, even if the argument is made that the inventions of Groups I and II share the technical feature of an antifreeze protein, according to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding special technical feature is a contribution over the prior art. In the instant case, antifreeze proteins have been shown by Duman (U.S. Patent No. 5627051; cited in the IDS) to lack novelty since Duman teaches a *D. canadensis* antifreeze protein (Example 1) as well as many others from different organisms (column 1, lines 54-61). Thus, even if it is assumed that the technical feature linking Inventions I-II is an antifreeze protein, this technical feature does not make a contribution over the prior art. Therefore, the claimed inventions do not meet the requirement of unity of invention under PCT Rule 13.2.

With regard to arguments that Group II should be examined because claim 13 has been searched by the International Search Authority, and its examination would not impose an undue burden on the Office, it is noted that (1) the basis for the restriction requirement as set forth by the previous Examiner is lack of unity and not burden of search on the Office, and (2) the present Examiner of record has to conduct a comprehensive search of all the claims at issue, including those previously searched by the International Search Authority, for examination to be complete as required by 37 CFR 1.104. In the instant case, a case for lack of unity has been presented, which is all that is required for a restriction requirement to be proper. In addition, while the Examiner is not arguing that the restriction requirement is proper since searching all of the claimed inventions would impose an undue burden on the Office, it is noted that searching all the inventions would require different patent/non-patent literature, as well as class/subclass searches which may not be co-extensive, therefore imposing an undue burden on the Office.

The requirement is deemed proper and therefore is made FINAL.

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Claim 13 is withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1-12, 14-20 are at issue and are being examined herein.

***Specification***

1. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See, page 6, lines 14-18. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

***Priority***

2. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/372,522 filed on 04/12/2002.

3. This application is the National Stage of PCT/CA03/00528 filed on 04/11/2003.

***Information Disclosure Statement***

4. The information disclosure statements (IDS) submitted on 10/7/2004 and 3/8/2007 are acknowledged. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

***Claim Objections***

5. Claims 1, 5, 14, 18 are objected to due to the recitation of “protein or a mimetic of the antifreeze protein or active fragment thereof”. For clarity, it is suggested that the “or” between “protein” and “mimetic” be replaced with a comma, and the term “thereof” be replaced with “of said mimetic”.

Appropriate correction is required.

***Claim Rejections - 35 USC § 112, Second Paragraph***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-12 and 14-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 1, 3-5, 7-8, 14, 18 (claims 2, 6, 9-12, 15-17, 19-20 dependent thereon) are indefinite in the recitation of “active fragment” for the following reasons. The claims are unclear and confusing absent a definition of the activity associated with the fragment. The term “active” can have many different interpretations to one of skill in the art. For example, one interpretation of the term “active” in regard to polypeptides is the ability to elicit antibodies. It is suggested that the term “active” be replaced with a term that clearly defines Applicant’s intended function. For examination purposes, no patentable weight will be given to the term “active”. Correction is required.

9. Claims 9 and 20 are indefinite in the recitation of “further comprising a second, different inhibitor” for the following reasons. While one of skill in the art would have assumed that the term “second” implies an additional inhibitor which is different from the one already present, it is unclear if the term “second, different” is (1) intended to further limit the nature of the second inhibitor, or (2) merely redundant. For examination purposes, it will be assumed that the term reads “further comprising an additional inhibitor”. Correction is required.

***Claim Rejections - 35 USC § 112, First Paragraph***

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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11. Claims 1-12 and 14-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As stated in MPEP 2111.01, during examination, the claims must be interpreted as broadly as their terms reasonably allow. As shown on page 12, lines 15-19, Applicant's definition of the term "mimetic" encompasses not only polypeptides but also small organic molecules which exhibit similar or enhanced thermal hysteresis activity as compared to the antifreeze proteins. Thus, the term "mimetic" includes any molecule which would have thermal hysteresis activity or antifreeze properties. In addition, as shown on page 10, lines 27-35, Applicant's definition of the term "derived" intends to encompass mimetics as well as any number of structural modifications. Therefore, the term "derived from X" does not further limit the antifreeze protein because a protein from source X having any number of modifications such that it has structure A cannot be distinguished from another protein isolated from source Y having the exact same structure A. In view of this interpretation, claims 1-12 and 14-20 encompass (1) a genus of antifreeze proteins having any structure, (2) a genus of molecules which have thermal hysteresis activity having any structure, (3) a genus of fragments of the antifreeze proteins of (1) or the molecules of (2) wherein said fragments have no thermal hysteresis, and (4) a method for inhibiting the formation or decreasing the rate of formation of clathrate hydrates using said genus of antifreeze proteins, molecules, and fragments. See, also, Claim Rejections under 35 USC 112, second paragraph for claim interpretation.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or]

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chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case, the claims as interpreted require a large genus of proteins/molecules which are functionally and structurally unrelated. The art discloses the structure of a few antifreeze proteins and some non-biological antifreeze agents are known in the art. However, the specification fails to provide any information as to (1) the structural elements required in any antifreeze protein, (2) the structural elements required in any molecule to show thermal hysteresis activity, (3) how to practice the claimed methods with fragments of molecules/proteins having thermal hysteresis activity which do not have that activity, (4) additional activities for those fragments which do not have thermal hysteresis, or (5) a correlation between structure and antifreeze activity.

Even if the claims were to recite a function for the genus of fragments required, the genus of polypeptides/molecules recited is a large genus with the potentiality of encompassing polypeptides/molecules having different structure. While one could argue that the structures of those proteins/molecules known in the art is sufficient to provide adequate description of all members of the genus, it is noted that the art recognizes different structural features associated with antifreeze activity. As known in the art and stated in the specification, different motifs have been found for antifreeze



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proteins. There is no evidence suggesting that these known motifs will be found in all antifreeze proteins yet to be discovered. Similarly, there is no evidence suggesting that all unknown molecules having thermal hysteresis will necessarily have those structural features known in the art to be associated with that activity. Therefore, since there is no additional information correlating structure with the desired function such that the structure of all antifreeze proteins/molecules can be described, one cannot reasonably conclude that those species known in the art provide adequate description of the entire genus of proteins/molecules.

Due to the fact that the specification and the art only disclose a few species of the genus recited, and the lack of description of any additional species by any relevant, identifying characteristics or properties, one of skill in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention.

12. Claims 1-12 and 14-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a winter flounder *P. americanus* type I antifreeze protein labeled wfAFP4 and/or a *C. fumiferama* antifreeze protein labeled CfAFP6, a method for inhibiting clathrate hydrate plug formation and a method for decreasing the rate at which clathrate hydrates reform, wherein said methods require said composition, does not reasonably provide enablement for (1) a composition comprising any antifreeze protein or any molecule that has thermal hysteresis, (2) a composition comprising a fragment of the antifreeze proteins or molecules of (1), wherein said fragments lack any antifreeze or thermal hysteresis activity, or (3) a method for inhibiting clathrate hydrate plug formation or a method for decreasing the rate at which clathrate hydrates reform, wherein said methods require the compositions or (1) or (2). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400 (Fed. Cir. 1988)) as follows: (1) quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence and absence of working examples, (4) the nature of the invention, (5) the state of prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The factors which have lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed in detail below.

***The breadth of the claims.*** Claims 1-12 and 14-20 are so broad as to encompass (1) compositions comprising any antifreeze protein or any molecule that has thermal hysteresis, (2) compositions comprising fragments of the antifreeze proteins or molecules of (1), wherein said fragments lack any antifreeze or thermal hysteresis activity, and (3) a method for inhibiting clathrate hydrate plug formation or a method for decreasing the rate at which clathrate hydrates reform, wherein said methods require the compositions or (1) or (2). See Claim Rejections under 112, second paragraph, and Claim Rejections under 112, first paragraph, written description, for discussion of claim interpretation and scope of the claims.

The enablement provided is not commensurate in scope with the claims due to the extremely large number of polypeptides and molecules of unknown structure and function encompassed by the claims. There is no structural limitation recited regarding the antifreeze proteins and mimetics thereof recited, and there is no description of the structural features which are associated with any antifreeze protein or mimetic thereof as recited. Thus, the genus encompasses compounds which the skilled artisan would not know how to make. In addition, there is no functional limitation recited regarding the fragments of polypeptides and mimetics thereof, and there is no disclosure as to the functions associated with said fragments. Thus, the skilled artisan would not know how to use them. In the instant case, the specification enables a composition comprising a winter flounder *P. americanus* type I antifreeze protein

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labeled wfAFP4 and/or a *C. fumiferama* antifreeze protein labeled CfAFP6, a method for inhibiting clathrate hydrate plug formation and a method for decreasing the rate at which clathrate hydrates reform, wherein said methods require said composition.

***The amount of direction or guidance presented and the existence of working examples.*** The specification discloses a composition comprising a winter flounder *P. americanus* type I antifreeze protein labeled wfAFP4 and/or a *C. fumiferama* antifreeze protein labeled CfAFP6, and shows the inhibition of clathrate hydrate formation as well as a decrease in the rate at which clathrate hydrates reform when this composition is used. However, the specification fails to disclose the structures of all the antifreeze proteins/molecules having thermal hysteresis activity encompassed by the claims, nor does it provide a structure/function correlation describing all the species encompassed by the genus of proteins/molecules recited. Furthermore, the specification is silent in regard to the structural modifications that can be made to any of the known antifreeze proteins to create mimetics retaining or enhancing the antifreeze activity.

***The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art.*** The amino acid sequence of a protein determines the structural and functional properties of that protein. Similarly, the structure of a molecule determines its functional properties. In the instant case, neither the specification nor the art provide a correlation between structure and activity such that one of skill in the art can envision the structure of any antifreeze polypeptide or the structure of any molecule having thermal hysteresis activity. As previously stated, the art, while teaching a few species of proteins/molecules having antifreeze/thermal hysteresis activity, fails to provide the structural elements common to all the species recited in the claims. As stated in the specification, and known in the art, there is more than one motif associated with known antifreeze proteins. Thus, one of skill in the art would not necessarily predict that those naturally-occurring antifreeze proteins not yet isolated will have the same motifs currently known in the art.

The art clearly teaches that changes in a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are required for that activity is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (Introduction to Protein Structure, Garland Publishing Inc., New York, page 247, 1991) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing *de novo* stable proteins with specific functions.

***The quantity of experimentation required to practice the claimed invention based on the teachings of the specification.*** While methods of generating or isolating variants of a polypeptide were known in the art at the time of the invention, it was not routine in the art to screen by a trial and error process for any number of polypeptides to determine which ones have antifreeze/thermal hysteresis activity. Similarly, while chemical synthesis methods exist for producing molecules having specific moieties, it was not routine in the art to screen by trial and error for any number of molecules to determine which ones have antifreeze/thermal hysteresis activity.

In the absence of (1) a structure/function correlation, and/ or (2) a rational and predictable scheme for structurally modifying those proteins/molecules known in the art such that the antifreeze/thermal hysteresis activity is maintained or enhanced, one of skill in the art would have to (1) test an infinite number of polypeptides/molecules to determine which ones have the desired activity, and (2) determine how to use those fragments that do not have any antifreeze/thermal hysteresis activity. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, as is the case herein, the specification must provide a reasonable amount of guidance with

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respect to the direction in which the experimentation should proceed so that a reasonable number of species can be selected for testing. In view of the fact that such guidance has not been provided in the instant specification, it would require undue experimentation to enable the full scope of the claims.

Therefore, taking into consideration the extremely broad scope of the claims, the lack of guidance, the amount of information provided, the lack of knowledge about a correlation between structure and function, the unpredictability of the art in regard to how structural changes affect function, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to practice the claimed invention. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

***Claim Rejections - 35 USC § 102***

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 1-4, 14-15, 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Klomp, U., (IBC Conference Proceedings, October 1997; cited in the IDS).

Claims 1-4 and 14-15 as interpreted are directed in part to a method for inhibiting clathrate hydrate formation wherein said method requires adding to hydrocarbons an antifreeze protein, and wherein said antifreeze protein contains a glycoprotein. Claims 18-19 are directed to a composition

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comprising an antifreeze protein wherein said antifreeze protein contains a glycoprotein. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation and Claim Rejections under 35 USC 112, first paragraph, written description, for discussion regarding the term “derived”.

Klomp, U. teaches the use of fish antifreeze glycoproteins (AFGPs) in a THF (tetrahydrofuran; a hydrocarbon) solution for inhibiting the formation of hydrates (pages 7-8). Thus, the teachings of Klomp, U. anticipate the instant claims as written.

15. Claims 1, 5, 9-10, 14, 16, 18, 20 are rejected under 35 U.S.C. 102(b) and 102(e) as being anticipated by Klomp et al. (U.S. Patent No. 5879561, issued 3/9/1999; cited in the IDS).

Claims 1, 5, 9-10, 14 and 16 are directed in part to a method for inhibiting clathrate hydrate formation or decreasing the rate at which clathrate hydrates reform, wherein said method requires adding to hydrocarbons any compound which would have antifreeze properties or thermal hysteresis activity as well as an additional inhibitor of clathrate hydrate formation, and wherein said inhibition occurs in a pipeline for oil drilling, exploration or transport. Claims 18 and 20 are directed in part to a composition comprising any compound which would have antifreeze properties or thermal hysteresis activity, and further comprises another inhibitor of clathrate hydrate formation. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation and Claim Rejections under 35 USC 112, first paragraph, written description, for discussion regarding the term “mimetic”.

Klomp et al. teach the use of alkylated nitrogen/phosphorous compounds (column 2, lines 38-44) in a solution comprising liquid hydrocarbons for inhibiting the formation of plugs by gas hydrates in steel pipelines (column 4, line 40-column 7, line 64). Klomp et al. also teach the use of an additional clathrate hydrate inhibitor (column 4, lines 12-27), and the use of the alkylated nitrogen/phosphorous compounds in a hydrate remelting operation mode (columns 5-6) where reformation of the hydrates was inhibited. Therefore, the teachings of Klomp et al. anticipate the instant claims as written.

*Claim Rejections - 35 USC § 103*

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 5-12, 16-17, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klomp, U., (IBC Conference Proceedings, October 1997; cited in the IDS) in view of Klomp et al. (U.S. Patent No. 5879561, issued 3/9/1999; cited in the IDS).

The teachings of Klomp, U. and Klomp et al. have been discussed above. Klomp, U. does not teach testing the fish antifreeze glycoprotein in a steel pipeline used in oil drilling/exploration/transport, in a conduit/machinery used in bacterial fermentation processes, or in a conduit/machinery used in disposal of CO<sub>2</sub>. Also, Klomp, U. does not teach testing the fish antifreeze glycoprotein for inhibition of clathrate hydrate reformation, or using an additional inhibitor of clathrate hydrate formation in combination with the fish antifreeze glycoprotein. Klomp et al. teach that fish antifreeze proteins and glycoproteins are effective in inhibiting clathrate hydrate formation (column 1, lines 54-62). However, Klomp et al. does not teach testing the fish antifreeze glycoprotein in a steel pipeline used in oil-related

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operations, in a conduit/machinery used in bacterial fermentation processes, or in a conduit/machinery used in disposal of CO<sub>2</sub>.

Claims 5-12, 16-17 are directed in part to a method for inhibiting clathrate hydrate formation or decreasing the rate at which clathrate hydrates reform, wherein said method requires an antifreeze protein as well as an additional inhibitor of clathrate hydrate formation, wherein the antifreeze protein comprises a glycoprotein, and wherein said inhibition occurs in a pipeline for oil drilling, exploration or transport, in a conduit/machinery used in fermentation processes, or in a conduit/machinery used in disposal of CO<sub>2</sub>. Claims 16-17 are directed in part to a method for decreasing the rate at which clathrate hydrates reform, wherein said method requires adding an antifreeze protein comprising a glycoprotein to hydrocarbons, and wherein said decreasing is due to inhibition of the memory effect. Claim 20 is directed in part to a composition comprising an antifreeze protein and an additional inhibitor of clathrate hydrate formation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to practice the method described by Klomp et al. with the fish antifreeze glycoprotein taught by Klomp, U. to inhibit the formation of clathrate hydrate formation or to decrease the rate at which clathrate hydrates reform in a pipeline used for oil-related operations, in a conduit/machinery used in fermentation processes, or in a conduit/machinery used in disposal of CO<sub>2</sub>. Also, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising the fish glycoprotein of Klomp, U. with the additional inhibitor of clathrate hydrate formation taught by Klomp et al. A person of ordinary skill in the art is motivated to practice such method because both Klomp et al. and Klomp, U. teach that the fish antifreeze glycoprotein works well in inhibiting the formation of clathrate hydrates, and the fish antifreeze glycoprotein is biodegradable. Since Klomp et al. and Klomp, U. teach that the fish antifreeze glycoprotein is effective in inhibiting the formation of clathrate hydrates, one of skill in the art would conclude that the fish glycoprotein is also able to decrease the rate at which clathrate hydrates reform. A person of ordinary skill in the art is motivated to use the method of Klomp et



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al. and Klomp, U. in conduit/machinery used in bacterial fermentation process or in disposal of CO<sub>2</sub>, because these processes may require the use of pipelines carrying water in contact with CO<sub>2</sub> at low temperatures. As taught by Klomp, U., CO<sub>2</sub> can form gas hydrates at low temperatures when in contact with water (page 1, first paragraph). In addition, a person of ordinary skill in the art is motivated to use a composition comprising the fish glycoprotein of Klomp, U. with the additional inhibitors of clathrate hydrate formation taught by Klomp et al. (e.g., N-vinyl-2-pyrrolidone polymers) for the benefit of increasing the inhibition effect on clathrate hydrate formation. One of ordinary skill in the art has a reasonable expectation of success at practicing the method of Klomp et al. and Klomp, U. with a composition comprising the fish glycoprotein and the additional inhibitor of clathrate hydrate formation since both Klomp et al. and Klomp, U. teach that the fish antifreeze glycoprotein is an effective inhibitor of clathrate hydrate formation, Klomp et al. teach the benefit of adding an additional inhibitor, and Klomp et al. teach the inhibition of clathrate hydrate formation and the decrease in the rate at which clathrate hydrates reform in a steel pipeline. Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made.

### ***Conclusion***

19. No claim is in condition for allowance.
20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).
21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally

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be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



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Art Unit 1652

DR

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